

(SEQ ID NO:26), A2 (SEQ ID NO:27)), B (B1 (SEQ ID NO:31), B2 (SEQ ID NO:32), C (C1 (SEQ ID NO:33), C2 (SEQ ID NO:34)), D (SEQ ID NO:37), E (SEQ ID NO:40)) and loops (AB1 (SEQ ID NO:28), AB2 (SEQ ID NO:29), AB3 (SEQ ID NO:30), CD1 (SEQ ID NO:35), CD2 (SEQ ID NO:36), DE1 (SEQ ID NO:38), DE2 (SEQ ID NO:39)) of interferon-beta-1a (SEQ ID NO: 25). See Example 1.

Please replace the pending sequence listing with the enclosed sequence listing.

In the claims:

Please cancel claims 25-40 without prejudice or disclaimer as drawn to a non-elected invention. Please amend claims 1, 5, 7-8, 15, 19 and 22, cancel claims 3-4, 9-10, 14, 16, 17 and 21, add new claims 41-48 and replace the pending claims with the following claims:

1. (Amended) A composition comprising the glycosylated interferon-beta-1a of SEQ ID NO: 25 coupled to a non-naturally-occurring polymer at an N-terminal end of said glycosylated interferon-beta-1a, said polymer comprising a polyalkylene glycol moiety.

2. The composition of claim 1, wherein the polyalkylene moiety is coupled to the interferon -beta by way of a group selected from an aldehyde group, a maleimide group, a vinylsulfone group, a haloacetate group, plurality of histidine residues, a hydrazine group and an aminothiols group.

5. (Amended) The composition of claim 1, wherein the interferon -beta-1a of SEQ ID NO: 25 is an interferon -beta-1a fusion protein.

6. The composition of claim 5, wherein the interferon -beta-1a fusion protein comprises a portion of an immunoglobulin molecule.

7. (Amended) A composition comprising the glycosylated interferon-beta-1a of SEQ ID NO: 26 coupled to a non-naturally-occurring polymer at the N-terminus of said glycosylated interferon-

beta-1a, said polymer comprising a polyalkylene glycol moiety.

35 8. (Amended) A physiologically active interferon-beta composition comprising a physiologically active interferon-beta-1a comprising the amino acid sequence of SEQ ID NO: 25 coupled to a polymer comprising a polyalkylene glycol moiety, wherein the interferon -beta- 1a is coupled to the polymer at a site on the interferon-beta-1a that is an N- terminal end, wherein the physiologically active interferon -beta 1a and the polyalkylene glycol moiety are arranged such that the physiologically active interferon-beta-1a in the physiologically active interferon -beta composition has an activity at least 2-fold greater relative to physiologically active interferon-beta-1b, when measured by an antiviral assay.

11. The composition of claim 8, wherein the interferon -beta-1a is coupled to the polymer at a site by way of a glycan moiety of the interferon -beta-1a.

12. The composition of claim 8, wherein the interferon-beta-1a is an interferon-beta-1a fusion protein.

13. The composition of claim 12, wherein the interferon-beta-1a fusion protein comprises a portion of an immunoglobulin molecule.

36 15. (Amended) A physiologically active interferon-beta composition comprising a physiologically active glycosylated interferon-beta-1a comprising the amino acid sequence of SEQ ID NO: 25 N-terminally coupled to a polymer comprising a polyalkylene glycol moiety, wherein the physiologically active interferon-beta-1a and the polyalkylene glycol moiety are arranged such that the physiologically active interferon-beta-1a in the physiologically active interferon-beta composition has equal activity relative to physiologically active interferon-beta lacking said moiety, when measured by an antiviral assay.

18. The composition of claim 15, wherein the interferon -beta is coupled to the polymer at a site by way of a glycan moiety on the interferon-beta.

a7 19. (Amended) The composition of claim 15, wherein the interferon-beta-1a is an interferon beta fusion protein.

20. The composition of claim 19, wherein the interferon beta fusion protein comprises a portion of an immunoglobulin molecule.

a7 22. (Amended) A stable, aqueously soluble, conjugated interferon-beta-1a complex comprising a interferon-beta-1a comprising the amino acid sequence of SEQ ID NO: 25 N-terminally coupled to a polyethylene glycol moiety, wherein the interferon-beta-1a is coupled to the polyethylene glycol moiety by a labile bond, wherein the labile bond is cleavable by biochemical hydrolysis and/or proteolysis.

23. A interferon-beta composition according to claims 1, 15 or 22, wherein the polymer has a molecular weight of from about 5 to about 40 kilodaltons.

24. A pharmaceutical composition comprising the interferon-beta composition of claim 23.

41. (New) The composition of claim 7, wherein the glycosylated interferon-beta-1a of SEQ ID NO: 26 is an interferon-beta-1a fusion protein.

42. (New) The composition of claim 41, wherein the interferon-beta-1a fusion protein comprises a portion of an immunoglobulin molecule.

a' 43. (New) A physiologically active interferon-beta composition comprising a physiologically active interferon-beta-1a comprising the amino acid sequence of SEQ ID NO:26 coupled to a non- naturally-occurring polymer at the N-terminus of said glycosylated interferon-beta-1a, said polymer comprising a polyalkylene glycol moiety wherein the physiologically active interferon-beta-1a and the polyalkylene glycol moiety are arranged such that the physiologically active interferon-beta-1a in the physiologically active interferon-beta composition has an activity at

least 2-fold greater relative to physiologically active interferon-beta-1b, when measured by an antiviral assay.

44. (New) The composition of claim 43, wherein the interferon-beta-1a is an interferon-beta-1a fusion protein.

45. (New) The composition of claim 44, wherein the interferon-beta-1a fusion protein comprises a portion of an immunoglobulin molecule.

46. (New) A physiologically active interferon-beta composition comprising a physiologically active glycosylated interferon-beta-1a, comprising the amino acid sequence of SEQ ID NO: 25, N-terminally coupled to a polymer comprising a polyalkylene glycol moiety, wherein the physiologically active interferon-beta-1a and the polyalkylene glycol moiety are arranged such that the physiologically active interferon-beta-1a in the physiologically active interferon-beta composition has equal activity relative to physiologically active interferon-beta lacking said moiety, when measured by an antiviral assay.

47. (New) The composition of claim 46, wherein the interferon-beta-1a is an interferon beta fusion protein.

48. (New) The composition of claim 47, wherein the interferon beta fusion protein comprises a portion of an immunoglobulin molecule.